Prenatal stress

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Results: Two hundred eigthy five (42%) subjects in the placebo group and 221 (32%) in the acarbose group converted to diabetes. The mean baseline level of WBC was 6.33 (SD 1.65) G/L and for ALT 31.70 (21.14) U/L. Only subjects with increased WBC levels had an elevated risk for diabetes (HR 1.44; p<0.001), but not subjects with elevated ALT levels (HR 1.10; p=0.36). In multivariate analysis with metabolic syndrome (NCEP III), treatment group, FPG, 2 hPG, HbA1C, triglycerides and WBC were independent predictors of newly diagnosed type 2 diabetes.
Conclusion: WBC but not ALT is a simple and routinely measured laboratory parameter which may be also used for risk estimation of developing diabetes. However, ALT could not be confirmed as independent risk factor in subjects with IGT.
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Effects of lifestyle modification on metabolic parameters and carotid intima-media thickness in patients with type 2 diabetes
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Background and Aims: Lifestyle modification is known to have positive effects on glycemic control and cardiovascular risk factors. Diabetes is a risk factor for cardiovascular disease. The carotid intima-media thickness (IMT) is considered to be an index of the progression of atherosclerosis. The aim of this study was to evaluate the effect of a 6 month lifestyle modification intervention on metabolic parameters and carotid IMT in patients with type 2 diabetes.
Materials and Methods: Sixty five patients with type 2 diabetes were randomly assigned into 2 groups, the lifestyle modification (LSM) group and the control (CON) group. The patients in the LSM group attended an intensive lifestyle modification intervention program for 16 weeks and had monthly meetings after the program. Patients in the CON group had no change in their usual treatment. Fasting plasma glucose, 2 hour postprandial glucose, HbA1c, lipid profiles, hsCRP, fasting insulin level, carotid IMT, blood pressure, and body indices were measured at baseline and after 6 months.
Results: LSM group showed a significant reduction in HbA1c (-0.98 ± 1.22 vs. +0.05 ± 1.24%, p=0.002), fasting plasma glucose (-28.72 ± 26.44 vs. +6.15 ± 44.91 mg/dl, p=0.022), and 2 hour postprandial glucose (–37.63 ± 44.79 vs. +14.77 ± 80.12 mg/dl, p=0.003) after 6 months. Total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, $HOMA_{IR}$, and hsCRP levels showed no significant difference. Body weight (–2.01 ± 2.59 vs. +0.22 ± 1.73 kg, p=0.001), BMI (–0.80 ± 1.00 vs. +0.02 ± 0.80 kg/m^2, p=0.003), systolic blood pressure (–8.15 ± 15.92 vs. +0.42 ± 14.07 mmHg, p=0.041) were significantly decreased in the LSM group. Significant carotid IMT regression was seen in the LSM group after 6 months (mean IMT: –0.050 ± 0.144 vs. +0.083 ± 0.167 mm, maximum IMT: –0.084 ± 0.197 vs. +0.07 ± 0.199 mm, p=0.004, p=0.009, respectively).
Conclusion: Lifestyle modification in patients with type 2 diabetes had positive effects on glycemic control, weight loss, and prevention of carotid atherosclerosis progression.

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The role of renin-angiotensin system blockers in the prevention of new -onset diabetes: meta-analysis of randomized controlled trials
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Background and Aims: Diabetes is associated with significant morbidity and mortality, especially when it is associated with cardiovascular disease. Prevention of diabetes will have significant impact especially among high risk patients.
Materials and Methods: We searched The Cochrane Controlled Trials Register (CCTR), MEDLINE, and EMBASE in January 2005. We included Randomized Controlled Trials (RCTs), in which outcomes of New -Onset Diabetes was reported. No language restrictions were applied. All identified trials were reviewed independently by two reviewers to determine whether trials should be included or excluded.
Results: Ten studies met inclusion criteria, including 77,541 participants. There was a statistically significant reduction in the incidence of New -Onset Diabetes in patients receiving Renin-Angiotensin System Blockers (ACEI or ARB) compared to other antihypertensive agents (RR 0.79; 95% CI 0.75–0.84, ARR=-0.02, NNT=50). There was a statistically significant reduction in the incidence of New-Onset Diabetes in patients receiving Renin-Angiotensin System Blockers compared to Diuretics, Conventional antihypertensive therapy (Diuretics or B-Blockers), and Calcium Channel Blockers (NNT=90,153, 62, respectively). There was a statistically significant reduction in the incidence of New-Onset Diabetes in patients receiving ACEI compared to Diuretics, and Conventional antihypertensive therapy. There was a statistically significant reduction in the incidence of New-Onset Diabetes in patients receiving ARB compared to other antihypertensive agents.
Conclusion: Renin-Angiotensin System Blockers significantly prevent the development of New-Onset Diabetes and should be utilized especially among high risk patients like patients with metabolic syndrome.

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Effects of a community-based intervention programme promoting physical activity on risk factors for diabetes and cardiovascular disease
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Background and Aims: Physical inactivity is an important risk factor for type 2 diabetes. Lifestyle intervention programmes focusing on diet and physical activity have documented that type 2 diabetes can be prevented in high-risk groups, but this approach is insufficient to stem the world wide epidemic of obesity and diabetes. Community-based strategies addressing the population at large are highly requested. We therefore designed an intervention study promoting physical activity on a district level in Oslo.
Materials and Methods: We selected the population in a low-income, urban district with high mortality rates and high prevalence of diabetes, obesity and physical inactivity for the intervention and the population in a neighbour district for controls. Baseline investigation of 2950 participants, 30–67 years old, follow-up investigation of 1776 (67% of those eligible). Of these 56% were women, 18% non-western immigrants. A set of theory-driven, low-cost intervention activities aimed at promoting physical activity was implemented in the intervention district from 2000 to 2003, tailored towards groups with different psychosocial readiness for change in physical activity. We used communication activities, invited to training sessions, labelled walking trails and offered a low-threshold fitness-test twice yearly. Main outcome measures were net changes observed between district cohorts in self-reported physical activity, psycho-social mediators related to physical activity, daily smoking, body weight, systolic blood pressure and serum levels of glucose and lipids.
Results: The net increase in physical activity as measured by two self-reported instruments was 9.5% (p=0.008) and 8.1% (p=0.02), and psychosocial mediators for change improved more (MANOVA, combined vector; P=0.002) in the intervention compared to the control district. The net proportion quitting smoking was 2.9% (95% confidence interval 0.1% to 4.0%, P= 0.043). The weight gain was less in the intervention district, with a mean net difference of 1.2 kg (0.6 to 1.9, P=<0.001) in men and 0.3 kg (–0.4 to 0.9) in women. Beneficial effects were also seen for the levels of triglycerides 0.16 mmol/l (0.06 to 0.25, P=0.002), cholesterol/HDL-cholesterol ratio 0.12 (0.03 to 0.20, P=0.007) and systolic blood pressure 3.6 mm (2.2 to 4.8, P<0.001), and in men also for the serum level of glucose 0.35 (0.03–0.67) mmol/l.
Conclusion: A community-based, low-cost intervention programme resulted in significant increase in physical activity in the intervention district followed by beneficial changes in several risk factors for diabetes and cardiovascular disease.
Support: The Norwegian Research Council

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Prenatal stress: effects on energy homeostasis and cognitive performance
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Background and Aims: The metabolic syndrome is a growing health problem in western industrialized societies. Whereas environmental factors, such as stress and diet, can propagate the aetiology of the metabolic syndrome during adulthood, one hypothesis states that they can also do so during the perinatal stage. For instance, exposure to stress during gestation is known to result in physiological, behavioral, and perhaps cognitive deteriorations during adulthood that finally lead to obesity and glucose intoler-

ance in aged rats. The changes in these parameters during young adulthood are largely unknown. Therefore, we investigated the influence of prenatal stress on energy balance, glucose homeostasis and cognitive performance in rats between 5 and 7 months of age.
Materials and Methods: Pregnant Wistar rats were subjected to immunological stress (LPS injections), psychological stress (chronic mild stress, CMS), or no stress at all. Body weight of the male offspring was measured regularly, and at age of 5 months, these rats were surgically equipped with jugular vein cannulas for blood sampling. To assess leptin sensitivity, the effect of a bolus leptin injection (25 ug iv) on food intake was measured. Intravenous glucose tolerance tests (IVGTT) and insulin sensitivity tests (IST) were performed to examine glucose homeostasis. After this, cognitive performance was tested in a novel object recognition test and an active shock avoidance test.
Results: CMS resulted in heavier male offspring, whereas LPS had no effect on offspring body weight. Neither CMS nor LPS caused major disturbing effects on glucose homeostasis. In fact, the CMS animals appeared to be more glucose tolerant during an intravenous glucose infusion. As opposed to the seemingly similar regulation of substrate homeostasis, CMS as well as LPS offspring performed less well in the "Novel Object Recognition" test (i. e., a standard cognitive performance task) relative to controls.
Conclusion: We conclude that perinatal stress differentially affects cognitive performance and regulation of energy balance in young adult offspring. Provided that perinatal stress leads to metabolic disregulation during ageing, the results in the present study demonstrate that metabolic disregulations are not required for the effects of prenatal stress on cognitive performance.
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Improved metabolic outcome and delayed structural rebuilding of pancreatic islets after regular intake of milk derivate in incipient diabetic Zucker rats (fa/fa)
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Background and Aims: Healthy nutrition is of key importance in preventing or even treating type 2 diabetes mellitus (T2DM). In this respect, the beneficial effects of probiotics have increasingly attracted public attention. The influence of a regular daily intake of a milk derivate (SMP) on the metabolic outcome and the progress of T2DM in Zucker rats (ZR, fa/fa) was studied.
Materials and Methods: Glucose-intolerante male fa/fa Zucker rats 15 weeks old were given daily either SMP in tap water ad libitum (25 g/l, SMP-group) or tap water alone(CO-group). Body weight, water and food intake and morning non-fasting blood glucose (BG) was determined weekly. Before, 3 and 6 weeks after treatment insulin, triglycerides and OGTT were monitored and 24 h blood glucose profiles were determined. At the end of the study pancreata were examined by immunohistochemistry and morphometry.
Results: SMP declined BG increase (5 weeks treatment: 6,1 ± 1,2 mmol/l vs. 7,5 ± 1,1 mmol/l in CO; $p<0,05$) and improved glucose tolerance (area under the curve, G-AUC after 6 weeks: 569 ± 145 vs. 780 ± 138 mmol x min/l; $p<0,05$). The insulin-AUC was increased with SMP (I-AUC: SMP=897 ± 120 vs. CO=745 ± 506 ng x min/l). The G-AUC correlated in SMP treated animals negatively with the portion of insulin producing cells in pancreatic islets ($r= -0,666$, $p< 0,05$), which was increased in SMP vs. CO (61,1 ± 4,7 vs. 51,9 ± 3,9%).
Conclusion: Daily intake of SMP in Zucker rats reduced insulin resistance, improved glucose tolerance and prevented structural rebuilding of pancreatic islets. This opens new avenues in the prophylaxis and / or treatment of metabolic syndrome and type 2 diabetes. The experimental results should be verified in clinical studies.

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Regulation of weight and obesity

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Mutation analysis of small heterodimer partner (SHP, NROB2) gene among 596 Chinese subjects and identification of four novel variants
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Background and Aims: The atypical orphan nuclear receptor small heterodimer partner (SHP, NROB2) modulates the transcription activity of MODY1 gene HNF-4α. Mutations in SHP were associated with moderate obesity among Japanese. The purpose of the study was to evaluate the prevalence of SHP variants among obese Chinese men.
Materials and Methods: We screened the whole coding region and intron/exon boundaries for SHP in 324 unrelated Chinese obese subjects (BMI 27.8 ± 2.7, BMI ≥25 kg/m^2 is the cut off for obesity in this study) and 272 unrelated nondiabetic and nonobese control subjects (BMI 20.3 ± 2.5, BMI <23 kg/m^2) by direct sequencing of the amplified polymerase chain reaction products.
Results: We identified six variants in 324 Chinese obese subjects, which included the previously reported mutations (H53fsdel10, R34X) in Japanese obese subjects. The H53fsdel10 was identified in seven separate obese carriers(2.2%) and R34X was identified in one carriers in this study. Additionally, a total of four novel mutations, including two missense mutations (G174A and G192E), one silent mutation (P10P) and one variants in intron1 (IVS1+10 C→T) were identified. The G174A and G192E variants were each identified in two separate obese carriers and P10P was identified in one carrier, the IVS1+10 C→T variants was also identified in one carrier. The overall frequency of the SHP mutations in Chinese obese objects in this study was 3.7% (12/324). All the mutations present in the heterozygous state. No mutations were identified in 272 nondiabetic lean controls ($P=0.00068$). Although, it was previously well documented that H53fsdel10 and R34X mutation were associated with obesity among Japanese, whether the four novel mutations have any functional significance needs further investigation.
Conclusion: Genetic variation in the SHP gene may be a key genetic factor responsible for moderate obesity among Chinese.
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Genetic interaction between the *IGF2* ApaI polymorphism and the insulin variable number of tandem repeats in their associations with body mass index in children
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Background and Aims: The insulin (*INS*) gene variable number of tandem repeats (VNTR) and single nucleotide polymorphisms (SNPs) in the nearby *IGF2* gene on chromosome 11 have been reported to be associated with weight gain. We therefore sought association between these genetic variants and weight at age 7 years in a normal population of children and explored possible gene-gene interactions.
Materials and Methods: Genomic DNA was extracted from blood and mouthwash samples from 1,400 children in the prospective Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC) birth cohort (the Children in Focus and control sub-cohorts). Of these 621 also had microsatellite-validated DNA samples from both their parents for transmission disequilibrium testing. Plasma IGF-2 concentrations were measured at age 5 years and heights and weights were measured at age 7 years. Body mass index (BMI) was calculated as weight (kg) divided by height (m)^2, and was converted into a standard deviation score (SDS) by reference to the full ALSPAC cohort (n~14,000). All samples were genotyped for *IGF2* ApaI (rs680; G+820A) and XcmI (rs3842759; A+6815T) (two *IGF2* SNPs reported to be associated with BMI in adults), and HphI (rs689) as a surrogate for *INS* VNTR class. Genotyping was performed by PCR followed by restriction fragment length polymorphism analyses.
Results: The *IGF2* XcmI SNP was associated with variation in plasma IGF-2 concentrations at age 5 years (geometric means: A/A 382 ng/ml, A/T 404, T/T 446; $p=0.001$) but not with markers of childhood obesity. In contrast both *IGF2* ApaI ($p<0.05$) and *INS* VNTR ($p<0.05$) were independently